

Amendments to the Specification:

Please note that the following amendments are made in reference to the substitute specification filed March 7, 2003.

Please replace the paragraph beginning at page 1, line 3, with the following rewritten paragraph:

--This application is a continuation of U.S. Patent Application Serial Number 08/974,549 filed November 19, 1997, Patent Number 6, 166, 178, which is a continuation-in-part application of U.S. Patent Application Serial Number 08/915,503, filed August 14, 1997, abandoned, ~~which is~~ and a continuation-in-part application of U.S. Patent Application Serial Number 08/912,951, filed August 14, 1997, Patent Number 6,475,789 and a continuation-in-part of application of U.S. Patent Application Serial Number 08/911,312, filed August 14, 1997, abandoned, all three of which are continuations-in-part of U.S. Patent Application Serial Number 08/854,050, filed May 9, 1997, Patent Number 6, 261, 836, which is a continuation-in-part of U.S. Patent Application Serial Number 08/851,843, filed May 6, 1997, Patent Number 6,093,809, which is a continuation-in-part of U.S. Patent Application Serial Number 08/846,017, filed April 25, 1997, abandoned, which is a continuation-in-part of U.S. Patent Application Serial Number 08/844,419, filed April 18, 1997, abandoned. This application also claims priority to Patent Convention Treaty Patent Application Serial No.: PCT/US97/17885 (published on April 9, 1998 as WO 98/14593) and to Patent Convention Treaty Patent Application Serial No.: PCT/US97/17618 (published on April 9, 1998 as WO 98/14592), both designating the U.S. and filed in the U.S. Receiving Office on October 1, 1997. Each of the aforementioned applications is explicitly incorporated herein by reference in its entirety and for all purposes. This application also incorporates by reference copending U.S. Patent Application Serial Number 08/974,584, filed November 19, 1997, in its entirety and for all purposes.--

Please replace the paragraph beginning at page 12, line 12, with the following rewritten paragraph:

~~--Figure 13, in two pages, shows~~ Figures 13A and 13B show the sequence of the DNA encoding the *Euplotes* 123 kDa telomerase protein subunit (*Euplotes* TRT; SEQ ID NO:109).--

Please replace the paragraph beginning at page 12, line 16, with the following rewritten paragraph:

~~--Figure 15, in five pages, shows~~ Figures 15A-15F show the DNA (SEQ ID NO:111) and amino acid (SEQ ID NO:112) sequences of the *S. pombe* telomerase catalytic subunit (*S. pombe* TRT).--

Please replace the paragraph beginning at page 12, line 26, with the following rewritten paragraph:

~~--Figure 20 shows, in seven pages,~~ Figures 20A-20E show the sequence of a nucleic acid with an open reading frame encoding a $\Delta 182$ variant polypeptide, with the sequence shown corresponding to SEQ ID NO:4. This Figure also shows the amino acid sequence of this $\Delta 182$ variant polypeptide, with the amino acid sequence shown corresponding to SEQ ID NO:5.
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Please replace the paragraph beginning at page 12, line 30, with the following rewritten paragraph:

~~--Figure 21 shows, in six pages,~~ Figures 21A-21E show sequence from an hTRT genomic clone, with the sequence shown corresponding to SEQ ID NO:6. Consensus motifs and elements are indicated, including sequences characteristic of a topoisomerase II cleavage site, NF κ B binding sites, an Alu sequence and other sequence elements.--

Please replace the paragraph beginning at page 14, line 3, with the following rewritten paragraph:

~~--Figure 35 shows, in four pages,~~ Figures 35A-35D show the DNA sequence (SEQ ID NO:115), as well as the amino acid sequences of all three open reading frames of the 43 kDa telomerase protein subunit from *Euplotes* (a = SEQ ID NOS:116-140; b = SEQ ID NOS:141-162; c = SEQ ID NOS:163-186).--

Please replace the paragraph beginning at page 14, line 7, with the following rewritten paragraph:

--~~Figure 36 shows~~ Figures 36A and 36B show a sequence comparison between the 123 kDa telomerase protein subunit of *Euplotes* (SEQ ID NO:187) (upper sequence) and the 80 kDa polypeptide subunit of *T. thermophila* (SEQ ID NO:188) (lower sequence).--

Please replace the paragraph beginning at page 14, line 10, with the following rewritten paragraph:

--~~Figure 37 shows~~ Figures 37A and 37B show a sequence comparison between the 123 kDa telomerase protein subunit of *E. aediculatus* (SEQ ID NO:189) (upper sequence) and the 95 kDa telomerase polypeptide of *T. thermophila* (SEQ ID NO:190) (lower sequence).--

Please replace the paragraph beginning at page 15, line 19, with the following rewritten paragraph:

--~~Figure 52 shows, in two pages,~~ Figures 52A and 52B show the DNA sequence of *tez1* (SEQ ID NO:111). Intronic and other non-coding regions are shown in lower case and exons (*i.e.*, coding regions) are shown in upper case.--

Please replace the paragraph beginning at page 16, line 4, with the following rewritten paragraph:

--~~Figure 58 shows~~ Figures 58A and 58B show the alignment of the M2 PCR product (SEQ ID NO:243) with *E. aediculatus* p123 (SEQ ID NO:242), *S. cerevisiae* (SEQ ID NO:244), and *Oxytricha* (SEQ ID NO:223) telomerase protein sequences. Also shown are the actual genomic sequences (SEQ ID NOS:246 and 249) and the peptides encoded (SEQ ID NOS:245 and 250), degenerate primers Poly4 (SEQ ID NO:238) and Poly 1 (SEQ ID NO:244), and homologous regions of the M2 PCR product (SEQ ID NO:247) and its encoded peptide region (SEQ ID NO:248).--

Please replace the paragraph beginning at page 16, line 24, with the following rewritten paragraph:

--~~Figure 64 shows~~ Figures 64A-64J show the alignment of the sequences from *Euplotes* ("Ea_p123") (SEQ ID NO:110), *S. cerevisiae* ("Sc_Est2p") (SEQ ID NO:222), and *S.*

pombe ("SP_Tlplp") (SEQ ID NO:112). In Panel A, the shaded areas indicate residues shared between two sequences. In Panel B, the shaded areas indicate residues shared between all three sequences.--

Please replace the paragraph beginning at page 17, line 1, with the following rewritten paragraph:

--~~Figure 68 shows, in four pages,~~ Figures 68A-68C show the DNA (SEQ ID NO:266) and amino acid (SEQ ID NO:267) of the ORF encoding an approximately 63 kDa telomerase protein encoded by the EcoRI-NotI insert of clone 712562.--

Please replace the paragraph beginning at page 17, line 9, with the following rewritten paragraph:

--~~Figure 71 shows, in two pages,~~ Figures 71A and 71B show the results of preliminary nucleic acid sequencing analysis of a hTRT cDNA sequence (SEQ ID NO:292).--

Please replace the paragraph beginning at page 17, line 11, with the following rewritten paragraph:

--~~Figure 72 shows, in ten pages,~~ Figures 72A-72I show the preliminary nucleic acid sequence of hTRT (SEQ ID NO:292) and deduced ORF sequences in three reading frames (a = SEQ ID NOS:293-320; b = SEQ ID NOS:321-333; c = SEQ ID NOS:334-342).--

Please replace the paragraph beginning at page 17, line 15, with the following rewritten paragraph:

--~~Figure 74 shows, in eight pages,~~ Figures 74A-74F show refined nucleic acid sequence (SEQ ID NO:343) and deduced ORF sequences (SEQ ID NO:344) of hTRT.--

Amendments to the Drawings:

The attached sheets of drawings include changes to the following drawings as indicated below:

Fig. 13 (2 sheets) are replaced with attached sheets Figs. 13A and 13B;
Fig. 15 (6 sheets) are replaced with attached sheets Figs. 15A-15F;
Fig. 20 (5 sheets) are replaced with attached sheets Figs. 20A-20E;
Fig. 21 (5 sheets) is replaced with attached sheets Figs. 21A-21E;
Fig. 35 (4 sheets) are replaced with attached sheets Figs. 35A-35D;
Fig. 36 (2 sheets) are replaced with attached sheets Figs. 36A and 36B;
Fig. 37 (2 sheets) are replaced with attached sheets Figs. 37A and 37B;
Fig. 52 (2 sheets) are replaced with attached sheets Figs. 52A and 52B;
Fig. 58 (2 sheets) are replaced with attached sheets Figs. 58A and 58B;
Fig. 64 (10 sheets) are replaced with attached sheets Figs. 64A-64J;
Fig. 68 (3 sheets) are replaced with attached sheets Figs. 68A-68C;
Fig. 71 (2 sheets) are replaced with attached sheets Figs. 71A and 71B;
Fig. 72 (9 sheets) are replaced with attached sheets Figs. 72A-72I; and
Fig. 74 (6 sheets) are replaced with attached sheets Figs. 74A-74F.

Attachment: Replacement Sheets